ANOVULATION IN CASES OF INFERTILITY

THESIS

FOR

M. S. (OBSTETRICS AND GYNAECOLOGY)

BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

1996 **ANJU RANI**

C E R T I F I C A T E

This is to certify that the work entitled "ANOVULATION IN CASES OF INFERTILITY", which is being submitted as a thesis for M.S.(Obstetrics and Gynaecology) Examination, 1996, Bundelkhand University Jhansi, has been carried out by Dr. Anju Rani under my direct supervision and guidance. The techniques embodied in this thesis have been undertaken by the candidate herself. The observations recorded were checked and verified by me from time to time.

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This is to certify that the work entitled "ANOVULATION IN CASES OF INFERTILITY" , which is being submitted as a thesis for M.S.(Obstetrics and Gynaecology) Examination, 1996, Bundelkhand University, Jhansi, by Dr. Anju Rani has been carried out in the department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi.

She has put in the necessary stay in the department as per university regulations.

Dated :

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A C K N O W L E D G E M E N T S

Whenever any piece of work is satisfactorily accomplished, it is never the work of one person but a number of people who silently work behind and go unheard off. With an overwhelming sense of gratitude I wish to acknowledge all those who made the completion of this thesis possible.

I am highly obliged and feel deeply honoured to express my profound sense of gratitude to my esteemed, learned and worthy guide Dr. S. Sharma, M.D., Assistant Professor, Department of Obst. & Gynaecology, M.L.B. Medical College, Jhansi for her excellent guidance, invaluable suggestions, untiring efforts backed by her unlimited knowledge. Her everhelping nature, constructive criticism, most perceptive mind and great sense of precision were constant source of inspiration during the course of this work. I shall remain indebted to her generosity for making available all facilities to work.

I am deeply indebted to my respected co-guide Dr. M. Kapoor, M.S., Associate Professor and Head, Department of Obst. & Gynaecology, M.L.B. Medical College, Jhansi for permitting me to conduct my study in the department . I am deeply grateful to her invaluable guidance, concrete and constructive suggestions, constant supervision and encouragement during the pursuit of this work.

I owe my sinceremost thanks to my respected co-guide Dr. Sunita Arora, M.S., Associate Professor, Department of Obst & Gynaecology, M.L.B. Medical College, Jhansi for her extreme co-operation, invaluable guidance to complete this work.

I am also grateful to Dr. Usha Agarwal, M.S., Associate Professor and Dr. Susheela Kharakwal, MD, Assistant Professor, Department of Obst. & Gynaecology, M.L.B. Medical College, Jhansi for their constant encouragement and suggestions during this study.

I am also grateful to Dr. Praveen Jain, M.D., for his extreme cooperation and invaluable help to complete this work. My special thanks to Dr. Ritu Jain, MD, who helped me a lot throughout the study.

I owe my special thanks to my parents,-in-laws for their kind and benevolent support. Words are inadequate to express my special thanks to my husband Dr. Sanjay Johri, M.D. for always keeping my morale high through words of encouragement and timely help in all aspects which destined this study to completion. I am thankful to my child who filled my hours of desparation with enthusiasm and inspiration.

I wish to acknowledge the kind and untiring support of my parents who taught me the meaning of perfection and in me their desire to achieve it so as I may be able to pursue my study with gust and confidence. The

debt I owe to my parents is supreme and can never be rapid in full throughout my life.

I extend my thanks to my colleagues who helped me in the completion of this study.

I am also thankful to Shri Phool Chandra Sachan, for his meticulous care and painstaking labour in preparing a neat type script of the present work.

Date : 28/7/96

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INTRODUCTION

INTRODUCTION

Inability to conceive after regular cohabitation without contraceptive protection for at least a period of one year is labelled as infertility. About 10-15% couples encountered this problem. In many cases an attributable causes like (1) male subfertility, (2) cervical, (3), uterine, (4) tubal, (5) ovarian, (6) endocrinologic or (7) immunologic factors can be identified.

In this study we are taking the problem of anovulation. The incidence of anovulation in cases of infertility is 12%.

The adult ovary goes through a cycle of activity which occupies approximately 28 days. It is not necessary that in every menstrual cycle in the life of woman ovulation has occurred, but it is generally accepted that in a woman with regular menstruation, the cycles are ovulatory. If the menstrual cycles are regular the possibility of anovulation is said to be 1 in 1000 (Vorys et al,1975). However, each woman tends to have her own menstrual rhythm.

The menstrual cycle commences on the first day of menstruation and has 2 phases (1) the ripening of an ovum which occupies that first 14 days follicular phase. During this period endometrial proliferation occurs and is the direct result of oestrogen influence. (2) The formation, function and early degeneration of the corpus luteum which occupies the

second 14 days - the luteal phase. Secretary activity and decidual reaction of the endometrium and manifestations of the luteal phase in the ovary are brought about by the progesterone acting in the presence of oestrogen. The two phases are separated by ovulation which makes the change over from the proliferative to the secretary phase in the endometrium. The duration of the luteal phase is more constant than that of the follicular phase and is generally reckoned as 14+2 days. Nevertheless it is subject to variation.

The srinkage of the endometrium premenstrually coincides with commencing failure of corpus luteum activity and is the direct result of the withdrawal of the supporting effect of oestrogen and progesterone.

Ovulation is a very important phenomenon in the reproductive life of a woman. It is the process by which an ovum in the form of secondary oocyte is discharged from the ovary to become a gamete. The ovary probable first sheds an ovum about the time of menarche but ovulation not usually stabilised as a regular occurrence with the age of 16-17 years. It then continues until the age of 45-50 years. Ovulation precedes the establishment of menstruation and sometimes occurs after the cessation of menstrual period.

A patient is considered anovulatory if after 2-3 months of observation no indices of ovulation have been identified or period of secondary amenorrhoea is 6 months or longer.

Ovulation can be detected by different parameters such as changes in cervical mucus, properties and its constituents, basal body temperature, serial vaginal smears, endometrial biopsy, essay of serum progesterone orurinary pregnendiol and other hormonal measurements.

Recently ultrasonography and various other modern techniques have been developed.

Daily vaginal smears, basal body temperature charting and cervical mucus requires careful monitoring of the patients over a long period of time. One can arrive at a definitive conclusion by the estimation of a rapid LH assay, but from a practical point of view these are expensive and not available in most clinics. Thus practical easy and inexpensive procedures for judging ovulation need to be evaluated.

The aims and objectives of the present study are :

1. To study the incidence of anovulation in infertile woman.
2. To find out etiological factors responsible for anovulation.
3. To find out the effect of treatment on anovulation.
4. To economise the detection of ovulation.
5. To find out the accuracy of the clinical and biochemical methods for detection of ovulation.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

The reproductive life of a woman depends entirely upon the phenomenon of ovulation. The reproductive process results from a complex series of interaction of hypothalamus, pituitary ovary and genital tract. Ovary plays the role in coordinating interactions of these component organs to bring about normal ovarian function.

Normal ovarian functions result in two major classes of product - sex steroid hromones and ova. Both are products of the follicular apparatus interacting with surrounding stromal elements under the stimulus of hormones secreted by pituitary which is controlled by the pituitary which is controlled in turn by hypophysiotrophic hormones (Rose and Wiele, 1974).

Disorders of ovulation are relative frequent and are responsible for infertility in about 15-20% of patients. These disorders include anovulation, oligo-ovulation and luteal phase defect (Moghissi and Wallach, 1983).

Corner (1927) was the first to suggest anovulatory menstrual cycles in women. Since then incidence of anovulation as a cause of infertility has been reported by various authors (Saha, 1961 and Israel, 1967). In a study of 291 infertile couples, anovulation was found to be the cause of infertility in 50.2% cases (Thomas and Forrest, 1980).

Such cycles in which an ovarian follicle matures to the point to rupture but fails to rupture and no corpus luteum is formed, was described by Novak. The presence of an anovulatory cycle or anovular amenorrhoea is physiological in women only at puberty and at menopause. However, it is an important cause of infertility. Anovulatory cycles alternating with normal cycles referred to as 'Oligo-ovulatory cycles' (Garcia and coworkers) are of relatively common occurrence.

Recent review concerning the mechanism of ovulation and its failure have been put forward by Bettendroff (1965), Betella (1967), Rennels (1967) and Wallach (1967) and are in agreement on the following principal factors.

Neurogenic: Various neurogenic or psychic alterations may be species (Horwalth, 1948, Ladowsky, 1967 and Mastumoto et al, 1968). A breakdown in the function of the hypothalamic sex centres causes anovulation.

Intrinsic alterations in the pituitary gland involving changes in the FSH and LH ratio may also cause anovulation.

Poor ovarian responsiveness undoubtedly leads to failure to ovulate. Sopena (1961) described the adnexitic ovary, in which the tunica albuginea cannot pierred owing to inflammatory fibrosis. Perhaps some similar situation is present in stein leventhal ovary (Greenblatt, 1961; Greenblatt et al, 1963). Mayer and Cochrane (1962) as well as Strassman (1945) have indicated

that premature death of the oocyte determined follicular atresia and inability to the follicle to rupture.

Koreman et al (1965) found increased testosterone levels in blood in patients with anovulatory cycles. Greenblatt (1961) observed occurrence of anovulatory cycles after prolonged androgen therapy and postulated that the same mechanism was involved in infertility owing to hyper-corticism. Lucis et al (1966) noted increased 17-keto-steroid values in cases with anovulatory cycle.

Netter et al (1966), Hochstaedt and Langer(1961) and Zener (1961) reported the occurrence of anovulatory cycles in association with the androgenital syndrome.

Severe hypothyroidism produces amenorrhoea hypogon-adism, hypogenitalium while moderate forms of hypothyroidism may be compatible with normal menses and normal genital development with no major changes other than anovulation.

Definite proof of ovulation is the establishment of pregnancy or the recovery of an ovum from the oviduct. Direct observation of a corpus luteum which the presence of a stigma by endoscopy or laprotomy is considered strong evidence of ovulation (Moghissi, 1980). Presumptive evidence may be obtained by assessment of corpus luteum hormones or their peripheral effect on the reproductive tract (Allende, 1956; Moghissi, 1980).

Determination of the precise time of ovulation has proven elusive since a long time, various techniques are commonly performed for detection of ovulation.

Progesteron stimulates endometrial gland maturation and decidual transformation of the endometrial stroma.

METHODS OF DIAGNOSIS

There is no single validated diagnostic tool that is both highly sensitive and specific in detecting ovulation. All existing methods suffer from major flaws.

I. TESTS BASED ON HORMONE ASSAY

1. Leutinizing hormone (LH)
2. Plasma and urinary oestrogens.
3. Serum progesterone of urinary pregnadiol.

II. TETS BASED ON PERIPHERAL AND SYSTEMIC CHANGES

1. Basal body temperature (BBT).
2. Cervical mucus.
3. Endometrial biopsy and dating.
4. Vaginal cytology.
5. Mittleschmerz
6. Premenstrual molimena

III. OTHERS METHODS OF OVULATION DETECTION

1. Salivary progesteron profile.
2. Cervical and vaginal glucose.
3. Endometrial receptors measurements - oestrogen and progesterone.
4. Immunohistochemistry.
5. Progesterone associated endometrial proteins(PEP).

6. Serum prolactin levels.

IV. SERIAL ULTRASONOGRAPHY

I. TESTS BASED ON HORMONAL ASSAY

Though these tests quite accurately predict the time of ovulation. They are rather expensive besides the fact that the facilities for these tests are not available at all the health centres and hospitals.

Serum estradiol demonstrates a characteristic peak approximately one to two days before LH peak (Ferin et al, 1973) and thirty seven hours prior to ovulation (Moghissi, 1980). Urinary estrogens reach maximum levels on the day or whithin one to two days of LH peak (Kohansson et al, 1971).

The preovulatory LH surge from pituitary as reflected in blood concentrations of LH is estimated to occur from 24 to 7 hours prior to ovulation (Yussman and Taymor, 1979). Younger et al (1978) described a rapid LH assay which they used to time artificial insemination. Regardless of technique used, the measurement of LH has proven useful in the detection of ovulation.

Plasma progesterone rises rapidly following ovulation reacting a peak at the mid luteal phase. Most workers found a critical level of 16 n mol/l (5 ug/ml) consistent with ovulation (Black et al, 1972; Shepared and Senturia, 1977).

Serum progesterone could also be measured by RIA in order to evaluate corpus luteum functions. Single

mid luteal values were recommended for this purpose. Rosa et al (1970) reported a midluteal progesterone value of 5 ng/ml or more as indicative of ovulation. Israel et al (1972) reported a value of 3 ng/ml in normal cycles Johanson (1972) suggested a minimum of 10 ng/ml. This variability in observations is due to pulsatile secretion and circadian rhythm of progesterone secretion (Filicori et al, 1984; Soules et al, 1988) and to the fact that mid luteal peak is short lived. An alternative was proposed by Daya (1989) - late luteal phase progesterone level in serum. It was found to be consistent specifically in discriminated value of 21 n mol/l on day 26. Abraham et al (1974) proposed that the sum of three mid luteal progesterone values should be considered as it was never less than 15 ng/ml.

Urinary pregnanediol measurements (Jones, 1949; Stanzyk et al, 1980 and Chatterton, 1982) and salivary progesterone profile (Li et al, 1989, Vuorento et al,1990) have been tried in an attempt to simplify total progesterone measurement in the luteal phase without consistent results and further studies are awaited.

II. TESTS BASED ON THE PERIPHERAL AND SYSTEMIC CHANGES

a. Basal Body Temperature (BBT)

The interpretation of BBT chart values on the progesterone mediated mid cycle shift of temperature. Attempts to quantify this have focussed on the magnitude

of temperature elevation. The rate of rise and the duration of temperature elevation before next menstrual period. Jones et al(1949) described BBT as being the most sensitive indicator of ovulation but a poor indicator of quality of ovulation. Gautray et al (1981) studied BBT charts in 88 women with LPD. A normogram had been previously constructed from 46 normal cycles. The luteal phase lengths of LPD patients were plotted in this. This analysis identified 2 groups of patients. (a) First group of 29 cases was within normal limits though the luteal phase length was often borderline. In all cases slow thermal rise to reach or exceed 37°C was measured. This period could extend over 2 days and in some cases lasted for 5 days. (b) Second group of 59 cases all fel outside the normal ellipse and showed wide variation in the lengths of both proliferative and luteal phases. Down and Gibson (1983) compared the luteal phases based on 3 BBT charts from each of 40 infertile women - 20 with LPD and 20 without LPD (proved by E.B.) They could not demonstrate any difference in the post ovulatory temperature rise between the two groups. Although the mean luteal phase length was significantly different)13.45 days in the non LPD and 11.8 days in LPD group).

b. Cervical Mucus

The changing pattern of ovarian steroid secretion affects the physical and chemical properties of cervical mucus which undergo cyclic changes in response to it.

(Marcus and colleagues, 1965; Moghissi and Wallach, 1983). These include changes in the morphology of cervix, viscosity and changes in chemical composition of mucus, spinbarkeit, ferning and midcycle mucorrhoea.

The influence of oestrogen production in the ovary on cervical mucus secretion was demonstrated by Seguy and Simmonet (1923) and others. Oestrogen stimulates by production of clear watery alkaline acellular mucus with intense ferning and spinbarkeit, whereas progesterone inhibits the secretions of cervical epithelia producing scanty, viscous opaque mucus with low spinbarkeit and absence of ferning (Zonde K and Rozin, 1954; Roland, 1962; MacDonald, 1969 and Epstein, 1978).

Seguy and Vimeux (1933) pointed out that during the intermenstrum, the cervical mucus becomes abundant watery clear with increased stretchability and can be drawn into the thread. This capacity of cervical mucus is related to spinbarkeit. This test becomes negative after ovulation.

Papanicolaou (1946) demonstrated that when the cervical mucus is spread on a glass slide and left to dry, it crystallizes with arborization. This phenomenon in most characteristic at the time of ovulation Rydberg (1948) described the pattern as fern like, hence the name palm like reaction (PL reaction).

Campos Da Paz (1953) showed that progesterone inhibits ferning. The test can remain positive in

anovulatory cycle until menstruation due to failing corpus luteum function, a phenomenon which can be utilized as a simple test for ovulation detection (Roland, 1952).

With preovulatory rise, the cervix softness and the os opens. After ovulation os closes again and cervix becomes firm and returns to a lower position (France, 1981). This showed that besides secretion of mucus oestrogen also acts on connective tissue and muscle of the cervix.

Anderson et al (1984) studied the change of cervical mucus peroxidase by spectroscopy as a method for ovulation detection.

A characteristic pattern of proteins is seen by immunoelectrophoresis at the time of ovulation (Heme et al, 1965). On the day of ovulation albumin, alpha anti-trypsin haptoglobin, lipoproteins, beta-transferrin and gammaglobulin were present, probably due to follicular rupture and discharge of its content through the fallopian tube, whereas only albumin or no protein was present before or after ovulation.

Birnberg et al (1958) studied the glucose levels in cervical mucus and found that maximum concentration occurred on the day of ovulation.

Most enzymes found in cervical mucus exhibit a cyclic pattern of a preovulatory decrease followed by post ovulatory rise (Skerlavay et al, 1968; Moghissi et al, 1976 and Takehisa, 1980).

c. Endometrial Biopsy

The uterine endometrium is known to demonstrate a predictable and rapid pattern of histological change over the menstrual cycle. Burch and Phelps (1943) wrote "The endometrium is the most valuable single indicator of ovarian activity in the human female and its histology. The most informative single criterion. In 1949 Jones recognized luteal phase deficiency as a clinical entity for the first time and proposed endometrial biopsy as the most quantitative test of corpus luteum function.

Noyes et al described 8 histological criteria used in dating of endometrium. Four pertaining to glandular epithelium (Pseudostratification of the nucleus vacuolation, secretion and mitosis) and four related to stromal changes (stromal edema predecidua, leukocyte infiltration and mitoses).

The histological dating of the luteal phase endometrium is then compared with chronological dating and a lag of more than 2 days is taken as luteal phase deficiency. The most advanced area of endometrium is taken for dating.

Chronological dating

It is done either retrospective or prospective.

Retrospective dating : It is based on the assumption of that luteal phase duration constantly 14 days irrespective of the length of the cycle. They day of ovulation is then determined by substracting 14 days from

theday of onset of next menses (NMP). The date of onset of next menses (NMP is taken as day 28 and the post ovulatory day on which EB was done is calculated by backdating from this.

Prospective dating : Day of ovulation is determined by BBT charts. LH surge or ultrasonographic follicular monitoring. Endometrial biopsy is then timed accordingly. The actual post ovulatory day is determined prospectively from the day of ovulation.

Endometrial biopsy is on of the most accepted methods but there are many variables affecting the results (a) timing of biopsy, (b) number of biopsy, (c) site of biopsy, (d) method used for chronological dating (e) interpretation of biopsy and inter and intra observer variation and (f) within subject between cycle variation.

a. Timing of biopsy : Early work by Brewer and Jones (1947) showed that biopsies done 4 to 6 days prior to menses most consistently reflected the overall status of the endometrium. According to Noyes and Haman (1953) endometrial dating when EB done on 20th day, Gautray et al(1981) 21st , 22nd and 23rd day to be optimal for endometrial biopsy.

Recently Johannisson et al (1987) did morphometric analysis using all indices and stercologic study of endometrium for the first time and measured DNA and RNA levels in endometrium. They stated that endometrial changes showed maximum significance around LH surge -2/-3 day

to LH +7/+8 day, where changes occurs with a high degree of regularity despite the length of pre and post ovulatory phases. Want Z et al (1980, 1984) observed that biopsies taken more than 6 days before menses were out of phase. more frequently. This suggested that endometrial biopsy should be taken 2-3 days prior to menses in order to avoid many false positive results. Some other studies (Soules et al, 1977, Dawns and Gibson, 1983, Shoupe et al, 1989) have also employed late luteal biopsies.

b. Number of biopsies : The required number of biopsies to be taken to firmly establish the diagnosis of LPD varies from one to three. Most studies have stressed on taking 2 biopsies to diagnose LPD (Jones et al, 1949, 1976; Soules et al, 1977; Ying et al, 1989).

c. Site of biopsy : The response to hormonal change is maximum in the superficial layers of fundus and upper anterior and posterior wall of the uterine(Falconer, 1947). The less vascular basal layer and lower segment endometrium lag behind and if biopsies are taken from these portions, there could be a higher possibility of out of phase biopsy (Wentz et al, 1980).

d. Method used for chronological dating : NMP has been traditionally used but it has many drawback. It is based on the presumption that luteal phase is of 14 days duration which has since been shown to be incorrect (Lenton et al, 1984, Johannison et al, 1987). Premenstrual spotting can confound the result if it is considered to be

the day of onset of menses. It has been postulated that endometrial biopsy could bring about earlier onset of menses probably by release of prostaglandins in the biopsy cycle.

There are various studies comparing retrospective dating with prospective methods of chronological dating. Noyes et al(1950, 1976) observed that only 38% of the women were in agreement ±2 days when histologic dating and NMP were correlated whereas 78% were in agreement when correlated with BBT. Li et al (1987) performed a study on 61 infertile women and concluded that the correlation between histologic dating and chronologic dating was found to be significantly better if the LH peak was used. Shoupe et al (1989) compared that four methods of chronologic dating NMP, BBT, LH surge and ultrasonographic monitoring when correlated with histologic dating by Noyes et al criteria in 13 parous women with normal cycles. They found NMP accurate in only 65.4% cases as compared to 76.9% with BBT, 84.6% with LH surge and 96.1% with ultrasonography.

e. Interpretation of biopsy : A lag of two or more days in histologic dating when compared to chronologic dating is considered to be sufficient to diagnose LPD in some studies) Thorney Croft, 1983, Ying et al, 1985, Tredway et al, 1987) whereas other believes in minimum lag of 3 days (Rosenfeld et al, 1980; Downs and Gibson, 1983 and Wentz et al, 1990).

Recently Davis et al (1989) found that in fertile women, 26.7% had sequentially abnormal biopsies when the criterion of lag of two or more days was used, whereas it was 5.6% when three or more days lag was the criterion.

f. Within the subject between cycle variation: Sporadic occurrence of LPD in some cycles in normal ovulating women has been repeatedly postulated (Aksael's 1980; Balasch et al, 1985 and Li et al, 1989).

COMPLICATIONS OF ENDOMETRIAL BIOPSY

These include excessive bleeding, pain, fever, vasovogal reaction and uterine perforation(Davidson et al, 1987). The more important complication is sampling in conception cycle. Rosenfeld et al (1975) observed that the likelihood of miscarriage is 10% and that of ectopic pregnancy 3%.

4. VAGINAL CYTOLOGY

Papanicolaou (1933) published the descriptions of variations in human vaginal smears during the menstrual cycle.

Though daily vaginal smear examination is necessary to pinpoint the time of ovulation (Riley et al, 1955; Allende, 1956; Jeffcoate, 1975) a single smear taken in the second half of the cycle reliably detects whether a corpus luteum has been formed (Jeffcoate, 1975). The progestational effects in vaginal smear in majority of cases permit a sound decision to be made whether ovulation

has occurred or not (Alende, 1956).

5. PREMENSTRUAL MOLININA

Premenstrual symptoms such as dysmenorrhoea breast tenderness, headache, mood changes, oedema together designated as premenstrual molimina occur almost exclusively in ovulatory cycles (Magyer et al, 1978). Anovular bleeding usually occurs unannounced.

6. MITTLESCHMERZ

It is the occurrence of lower abdominal pain near the time of ovulation. The exact aetiology is unknown, but it may be due to muscular cramps in uterus, tubes or large bowel (Jeffcoate, 1975). 'O' Herliky et al (1980) noted that the pain coincides with the day of peak plasma LH.

7. LUTEAL PHASE LENGTH

It is calculated from the day of ovulation to the day of onset of menses. Traditionally a luteal phase less than 10 days is considered to be short. Down and Gibson (1983) compared luteal phase length of LPD and Non LPD patients based on BBT chart and observed that a luteal phase less than 11 days represented an abnormal cycle per se as well controls had longer cycle lengths. These observations support the concept that short luteal phase represents a more extreme form of LPD and taken alone. Luteal phase length is not a sensitive method of diagnosing LPD.

Hyperproteinaemia has been known to be associated with LPD (St. Michael and Dizerega, 1983) and the encouraging response of such patients to bromosriptive has been documented years ago (del Pozo, 1979).

IV. SERIAL ULTRASONOGRAPHY

Real time ultrasonography is a relatively new imaging technique which means it is now possible to follow the follicular events directly in addition to diagnosing other gynaecological problem like fibroid, endometriosis and genital abnormalities.

The role of serial ultrasonography in detecting ovulation has been well established by various studies ('O' Herlihy et al, 1980; Queenan et al, 1980; Marinno et al, 1982; Wetzel and Hoogland, 1982; Eissa et al, 1986). Shoupe et al (1989) has clearly demonstrated the accuracy of serial transvaginal sonography used for chronological dating when correlated with histologic dating. In addition daily follicular monitoring aids us in identifying the subgroups of LPD patients with abnormal folliculo-dynamics so that appropriate therapy can be instituted (ovulation induction).

Abnormal folliculogenesis is 12-19% demonstrated by different studies has been defined in these studies as (1) Rupture of small follicle size (⩽17 mm), (2) rupture after abnormal growth (⩽1 mm/day for 3 days or plateau in growth for 2 days prior to rupture), (3). Leutinised unruptured follicles.

Ying et al (1987) studied 39 patients with LPD and found that only 46% has normal sized follicles, 39% had small follicles and 15% had leutinised unruptured follicles. Hamilton et al (1990) reported a much higher percentage of cases with luteal cyst formation among infertile women nearly 50%.

Lutinized unruptured follicle syndrome (LUFS)

Follicles fails to rupture after undergoing apparently normal or abnormal follicular development. It has been repeatedly postulated as a cause of infertility (Marik and Hulka, 1978) and Portuondo et al, 1981). The prevalence of LUFS by laparoscopy performed 2-4 days after presumed day of ovulation (using BBT/LH surge) varied widely 6 to 79% in infertile women (Koninckx et al, 1980) as high as 47% in fertile women (Vonrell et al, 1982).

Serial ultrasonography provides a potential alternative being non-invasive early reproducible and cost effective in diagnosing LUFS (Daly OC, 1985). The incidence of LUFS by ultrasonography is roughly 10% in infertile women (Gibson et al, 1984 - 10%, Daly et al, 1985-9%, Check et al, 1984-8%, Ying et al, 1987 - 15%) however a recent report by Hamilton et al (1990) found 45% incidence of luteal cyst.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was carried out in the Department of Obstetrics and Gynaecology, with active collaboration with the department of Pathology, M.L.B. Medical College, Hospital Jhansi over a period of one year for the assessment of anovulation in female infertility.

SELECTION OF CASES

The study comprised of patients attending the outdoor clinic of the department of Obstetrics and Gynaecology for infertility either primary or secondary with regular and irregular menstrual cycles and patients of secondary amenorrhoea.

CLINICAL EXAMINATION

A detailed history was taken in each patient followed by thorough general, systemic and local examination as per the following proforma.

Name : Age :

Address :

HISTORY

Total duration of consumation of marriage :

Menstrual patterns : 1. Premenstrual

2. Postmenstrual spotting.

H/o premenstrual tension.

H/o midcycle pain and wetting.

H/o Hypothermia.

Obstetric History : Abortion/Cesation

H/o becoming over due then bleeding

TREATMENT HISTORY

H/o taking oral contraceptive or any drug suppressing ovulation

H/o taking ATT, cortisone

FAMILY HISTORY

Diabetes

Sterility

HISTORY OF ASSOCIATED DISEASES

Symptoms of hyperprolactinaemia

Symptoms of diabetes mellitus

Symptoms of hypothyroidism.

EXAMINATION

General : Pulse

Hair growth

Skin texture

Thyroid swelling.

General features (Androgenicity)

Hirsutism

Secretion

Systemic

P/V

Uterus

Condition of ovaries

Size of ovary

Cervical mucus (according to day of examination)

INVESTIGATIONS

General : Hb gm%, TLC : DLC :

E.S.R. : V.D.R.L. :

Blood sugar : Fasting mg% PP: mg%

B.B.T.

Cervical mucus examination & ferning

Endometrial dating

M.I.

Hormonal assay : Thyroid

LH

FHS

Prolactin

Causes of infertility were done as :

- 7th day tubal testing.
- 10th day hysterosalpingography.
- 20th day cervical mucus and

Husband seminogram.

ENDOMETRIAL BIOPSY

An endometrial currette used for taking the biopsy from the endometrial cavity

PREPARATION OF PATIENT

The patient was asked to come in the premenstrual phase. A written consent of the patient or her attendants was taken. The patient was asked to evacuate her bladder.

INSTRUMENTS USED

Sponge holding forceps

Anterior vaginal wall retractor

Catheters

Sinus speculum

Volsellum

PRESERVATIVE : Absolute alcohol or 40% formaline solution.

STAIN : Haemotoxylin and Eosin were used.

ANAESTHESIA : IV sedation with fortwin and phenergon.

METHOD

- Patient was put in lithotomy position.
- Vilva painted and drapped.
- Bladder was catheterised in those cases where it was not already evacuated.
- Bimanual pelvic examination was done to ascertain the position of the uterus and adenexa.
- Sinus speculum was inserted and the cervic was visualised with the help of anterior vaginal wall retractor.
- The anterior lip of the cervix was caught hold by a volsellum.
- Uterine sound was passed to know the length of the uterine cavity and to exclude uterine polyp.
- Endometrial biopsy was taken by means of endometrial biopsy currette and tissue obtained was preserved and in absolute alcohol or 40% formaline solution.
- Local antiseptic lotion was applied over cervix.

PREPARATION OF TISSUE FOR HISTOPATHOLOGICAL EXAMINATION

Dehydration of Tissue

Pieces are cut and subjected to the process of dehydration in the automatic processor. Dehydration is done by putting tissues in increasing concentration of alcohol. The extra amount of water was soaked by bloatting paper.

Clearing of Tissue

After dehydration, tissue was cleared in xylene. The tissue was embedded in paraffin wax which was allowed

to set.

Blocking of Tissue : The tissue was blocked in cubical moulds by placing two metallic angles (L forms).

Section cutting : Section was cut at 5-6 micrometer thickness with the help of rotating microtone.

Staining

Tissue was deparaffinased and subjected to the steps of Harris haematoxylin and Eosin staining followed by mounting in OPX.

The slide was examined under high power and endometrium was then phased finally, clinical and histopathological findings were correlated.

CERVICAL MUCUS

Samples of cervical mucus were collected during selection period of menstrual cycle i.e. in post ovulatory period to see the ferning is present or not.

Patient was laid in lithotomy position. Part was painted and drapped. A sterile unlubricated speculum was used and the anterior lip of cervic cought hold by a volselum. The area around the external os was wiped with absorbent dru cotton wool, mucus was aspirated with an insulin syringe (without needle). The nozzle of the syringe was inserted as high as possible into the endocervical canal and withdrawn until the external os was reached

and the suction then released to avoid contamination of the endocervical specimen with vaginal content. Then spread to the slide and allow to dry. It was difficult to separate the upper from the lower contents of endocervical canal so the entire specimen was examined.

Cervical mucus was studied for the following things :

1. Viscosity

Because of the small quantities involved the viscosity was evaluated in terms of 1+ to 4+.

1+ : Normal mid cycle mucus.

4+ : Thick, viscous premenstrual mucus.

2. Spinbarkeit (Spinability)

The length of the mucus thread stretched between a glass slide and coverslip was measured in centimeters immediately after collection of the samples.

3. Fern Test

Ferning was recorded as :

1+ : Linear (minimal degree of oestrogen effect)

2+ : Having some palm leaf appearance with arborisation of the leaves at 90° to each other.

3+ : Having moderate degree of arborisation when the palm leaf appearance involves angulation at three right angles.

4+ : Showing maximal arborisation where the palm leaves appear at four angles to each other.

BASAL BODY TEMPERATURE (BBT)

Temperature was recorded daily orally under standard condition before rising from bed in the morning and before eating or drinking.

Body temperature is raised by progesterone and is therefore higher during the luteal phase of the cycle and also during pregnancy during the follicular phase and later parts of menstrual flow. The temperature was relatively low.

Ovulation is sometimes preceded by a low peak and is generally followed by a rise. The rise may occur suddenly within 24 hours or gradually during 4 days. After this temperature remains 0.2-0.5^{o} higher than in the follicular phase until the onset of next period.

ULTRASONOGRAPHY

The modern real time ultrasonic apparatus has been used to describe ovarian and follicular characteristics throughout spontaneous and stimulated ovulatory cycles. This is helpful in the induction and confirmation of ovulation, artificial insemination and in vitro fertilization.

The size of the dominant follicle can be followed to the time of ovulation. During the 4 to 5 days prior to ovulation the follicle grows rapidly in a linear manner by about 2 to 3 mm a day reaching a mean diameter of around 20-24 mm by the time of ovulation. Although the wide range in the diameter of the preovulatory follicle precludes its

use as a single index for the prediction of ovulation. Several other preovulatory sonographic features have been described.

1. Separation of hypervascular edematous thecal tissue from the granulosa cell layer. These can be detected by the appearance of a line follicle. This feature is consistently seen within 24 hours of ovulation.
2. Another sign of developing follicular maturity is the detection of a small echogenic area projecting into the follicle which represents the cummulus oophorus. It confirms that a cystic structure is needed an oocyte containing follicle and ovulation will occur within 36 hours.

Patient came 3-4 days prior to suspected ovulation The serial ultrasonography done on alternate day till ovulation occurs or follicle mature too much but ovulation was not occur as in lutinized unruptured follicle syndrome. It shows following features :

1. Persistence of a dominant follicle with an echo free cystic appearance beyond 36 hours after the LH peak with no evidence of collapse.
2. In LUF normally sharp definition between the follicle wall and follicle fluid becomes an ill defined gray zone echoes.

Most of these cysts decrease in size with the peripheral echogenic zone progressively encroaching into

the centralcystic area over 2-4 days to form an apparently normal corpus luteum.

HORMONAL ASSAY

Hormonal assay for LH, FHS serum prolactin and thyroid hormones done for some cases. For detection of ovulation, LH and FHS have limited role because they are very costly for our surrounding population. Other simpler method was used to detect ovulation.

Serum prolactin and thyroid hormone assay was done to detect the other disorder which may leads to anovulation and infertility.

O B S E R V A T I O N S

O B S E R V A T I O N S

Fifty cases of infertility and secondary amenorrhoea were studied during the period of 1 year in the out patient department of Obstetrics and Gynaecology, M.L.B. Medical College, Hospital, Jhansi.

TABLE I : Showing distribution of cases according to chief complaints.

Chief complants	No.of cases	Percentage
Primary infertility	40	80.0
Secondary sterility	8	16.0
Secondary amenorrhoea	2	4.0

Table I shows the distribution of cases according to the chief complaints. Maximum number (80%) of cases complained of primary sterility.

TABLE II : Showing the distribution of cases according to their age.

Age groups (years)	No.of cases	Percentage
16 - 20	11	22.0
21 - 25	24	48.0
26 - 30	12	24.0
31 - 35	3	6.0
36 - 40	1	2.0

TABLE Table II shows the distribution of cases according to age. Maximum number (48%) of cases belonged to the age group of 2 25 years and the minimum 1(2%) case was from 36-40 years of age group.

TABLE III : Showing distribution of cases in relation to socio-economic status.

Socio-economic status	No.of cases	Percentage
I. Upper	-	-
II. Upper middle	4	8.0
III. Lower middle	27	54.0
IV. Upper lower	9	18.0
V. Lower	10	20.0

Table III shows that the majority of cases belonged to the lower middle socio-economic group (54%) and remaining cases belonged upper lower and lower status i.e. 18 and 20% respectively. Though infertility is known to be more common in the higher socio-economic status, the higher incidence in the middle and lower status is because general population around Jhansi mostly belonged to these groups. Besides the people belonging to higher classes , do not frequent to routine OPD but go to private treatment.

TABLE IV : Showing the distribution of cases according to religion.

Religion	No.of cases	Percentage
Hindu	44	88.0
Muslim	4	8.0
Christian	1	2.0

Table IV shows the distribution of cases according to religion. Maximum number (88%) xcases were Hindus followed by 8% cases from Muslim religion and the least only one case was from Christians.

TABLE V : Showing distribution of cases according to inhabitants of rural or urban areas.

Area	No.of cases	Percentage
Urban	26	52.0
Rural	24	48.0

Table V shows the distribution of cases according to inhabitants of urnam and rural areas. The number of cases in both the groups were approximately the same i.e. urban and rural residents were 52% and 48% respectively. Thus it is evident from the table V that the infertility was equally common in both urb and rural population.

TABLE VI : Showing distribution of cases according to menstrual patterns.

Menstrual pattern	No.of cases	Percentage
Polymenorrhoea	4	8.0
Normal	36	72.0
Oligomenorrhoea	8	16.0
Amenorrhoea	2	4.0

Table VI shows that 4 cases had polymenorrhoea, 36(72%) cases had normal menstrual cycle and 8(16%) cases had oligomenorrhoea and the minimum 2(4%) cases had amenorrhoea. Maximum number (72%) had normal menstrual cycle.

TABLE VII : Showing distribution of cases according. to menstrual pattern and sterility.

Menstrual pattern	Primary sterility		Secondary sterility	
	No.	%	No.	%
Polymenorrhoea (4)	4	100.0	-	-
Normal (36)	30	83.0	6	17.0
Oligomenorrhoea (8)	6	75.0	2	25.0
Secondary (2) amenorrhoea	1	50.0	1	50.0

Table VII shows the distribution of cases of different menstrual patterns according to the type of infertility. All the 4 cases of polymenorrhoea complained of primary infertility (100%).

Out of 36 cases having normal menstrual cycle, 30(83%) suffered from primary infertility while remaining 6(17%) cases suffered from secondary infertility.

6 out of 8 cases of oligomenorrhoea had primary infertility (75%) while 2(25%) cases had secondary infertility.

2 cases of secondary amenorrhoea suffered from primary and secondary infertility 1 case each.

TABLE VIII : Showing distribution of cases according to duration of infertility.

Duration (Years)	No.of cases	Percentage
1 - 5	27	54.0
6 - 10	18	36.0
10 - 15	5	10.0
16 - 20	2	4.0

Table VIII shows the duration of infertility Maximum number (27, 54%) cases were presented with sterility of 1-5 years duration and the minimum 2(4%) cases presented with seterility of 16-20 years duration.

TABLE IX : Showing the distribution of cases according to P/V examination.

Menstrual pattern	Hypo-uterus 6 cm No. (%)	Normal size uterus No. (%)	Palpable ovary		Cystic ovary	
			Single No. (%)	Both No. (%)	Single No. (%)	Both No. (%)
Polymenorrhoea	1 (25)	3 (75%)	-	-	-	-
Normal	3 (8.33)	30 (83.3)	2 (5.5)	1 (2.7)	1 (2.7)	-
Oligomenorrhoea	2 (25)	5 (62.5)	1 (12.5)	-	-	-
Secondary Amenorrhoea	1 (50)	1 (50)	-	-	-	-

Table IX depict the important findings on per vaginal examination. Hypoplastic uterine (less than 6 cm uterocervical length) were found in 1(25%) case of polymenorrhoea. 3(8.33%) cases with normal menstrual cycle, 2(25%) of oligomenorrhoea and 1(50%) cases with secondary amenorrhoea. One ovary was palpable in 2(5.5%) cases with normal menstrual cycle and 1(12.5%) cases of oligomenorrhoea. Both ovaries were palpable in only one cases of normal menstrual cycle. One ovary was found cystic in 1(2.7%) case with normal menstrual cycle.

TABLE X(A) : Showing distribution of cases according to premenstrual dysmenorrhoea.

Ovulatory pattern	Pain		No. pain	
	No.	%	No.	%
Ovulatory (36)	21	58.33	15	41.67
Anovulatory (10)	2	20.00	8	80.00

Table X(A) shows that premenstrual dysmenorrhoea was present in 21(58.33%) cases of ovulatory and 2(20%) cases of anovulatory patients. So this is more associated with ovulatory infertility.

TABLE X(B) : Showing distribution of cases according to other premenstrual molimina.

Ovulatory pattern	Breast tenderness		Abdominal fullness		Headache	
	No.	%	No.	%	No.	%
Ovulatory (36)	8	22.2	10	27.77	1	2.7
Anovulatory(10)	1	10.0	1	10.0	-	-

Besides pain other menstrual molimina are shown in table X(B). Breast tenderness was present in 8(22.22%) cases of ovulatory as against 1(10%) case of anovulatory patients.

Abdominal fullness was experienced by 10(27.77%) and 1(10%) cases of ovulatory and anovulatory patients respectively.

Headache was found in only 1(2.7%) cases of ovulatory patients and it was totally absent from anovulatory

cycle. Mittleschmerz was found in only 1(2.7%) case.

TABLE XI(A) : Showing distribution of cases according to endometrial biopsy findings.

E.B. findings	No.of cases	Percentage
Secretary	36	72.0
Proliferative	10	20.0
TB endometritis	2	4.0

Endometrial biopsy wad done in all cases of premenstrually or on first day of period. Out of all 50 cases, 36(72%) cases showed secretary endometrium and 10(20%) cases showed proliferative endometrium.

The incidence of T.B. endometrium was present in 2(4%) cases of present study.

TABLE XI(B) : Showing distribution of cases according to menstrual pattern and ovulation as seen by endometrial biopsy.

Menstrual pattern	Ovulatory		Anovulatory	
	No.	%	No.	%
Polymenorrhoea (4)	3	75.00	1	25.00
Normal (36)	27	75.00	8	22.22
Oligomenorrhoea (8)	5	62.50	3	37.50
Secondary amenorrhoea(2)	-	-	1	50.00

Table XI(B) shows overall incidence of ovulation as seen by endometrial biopsy in polymenorrhoea. Ovulation was found in 3(75%) cases and anovulation in 1(25%) case.

In oligomenorrhoea, 5(62.5%) cases showed ovulatory and 3(37.5%) cases showed anovulatory pattern. In cases with normal menstrual cycles ovulation was found in 27(75%) cases and anovulation in 8(22.22%) cases. One (50%) case cases of secondary amenorrhoea showed anovulatory pattern and in one case no opinion could be made

TABLE XII(A) : Showing distribution of cases according to cervical mucus viscosity in relation to anovulation.

Ovulation pattern	Viscosity					
	Low		Moderate		High	
	No.	%	No.	%	No.	%
Ovulatory (36) premenstrual	30	83.33	5	13.80	1	2.7
Anovulatory (10) Premenstrual	-	-	2	20.00	8	80.00

Table XII(A) shows that cervical mucus examination at 14th day. Viscosity in premenstrual period was low in 30(83.33%) cases, moderate in 5(13.8%) and high in 1(2.7%) cases. of ovulatory patients with infertility.

Viscosity in anovulatory infwrtility was seen high in 8(80%) and moderate in 2(20%) cases.

TABLE XII(B) : Showing distribution of cases according to ferning property of cervical mucus in relation to ovulation pattern.

Ferning arborization	Ovelation pattern(Premenstrual)			
	Ovulatory (36)		Anovulatory(10)	
	No.	%	No.	%
+4	-	-	6	60.00
+3	1	2.77	3	30.00
+2	2	5.55	1	10.00
+1	4	11.11	-	-

M Table XII(B) shows that ferning was of high grade +4,+3 in anovulatory infertility and in ovulatory infertility it shows 11.11%, 5.55% and 2.77% in +1, +2 and +3 respectively and the rest 80% of patients with ovulatory infertility showed no ferning at all.

TABLE XIII : Showing distribution of the cases for detection of anovulation by ultrasonography in comparison with endometrial biopsy.

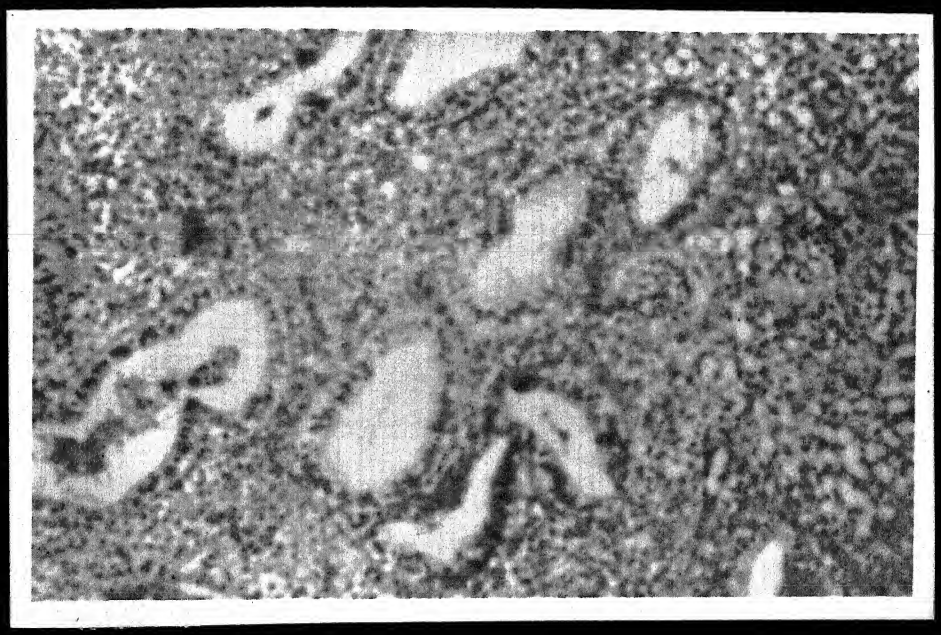
Type of endometrium		On ultrasonography			
		Ovulatory		Anovulatory	
		No.	%	No.	%
Secretary	(36)	35	97.22	1	2.77
Proliferative	(10)	-	-	10	100.00

Table XIII shows that there is not much difference in detection of ovulation by ultrasound and endometrial biopsy. In secretary type of endometrium, 35(97.22%) cases had ovulation and only 1(2.77%) had anovulatory cycles. In proliferative types of endometrium all 10 cases did not ovulate.

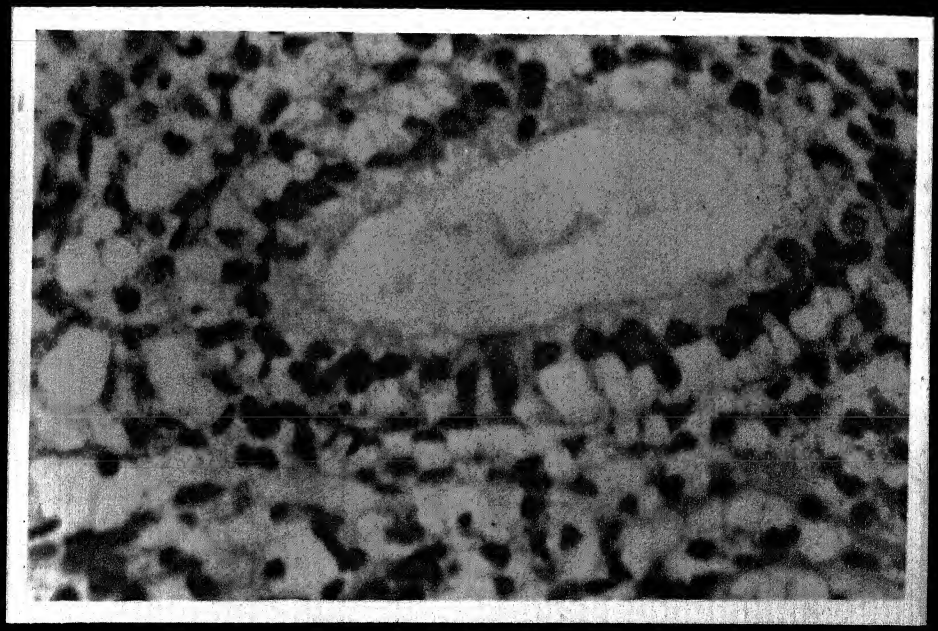
Two cases conceived during the course of study who were taking the treatment for anovulation.

With further investigations 2 patients were found to have hyperprolectienemia who were given treatment for it. Out of 2, 1 (50%) conceived during treatment.

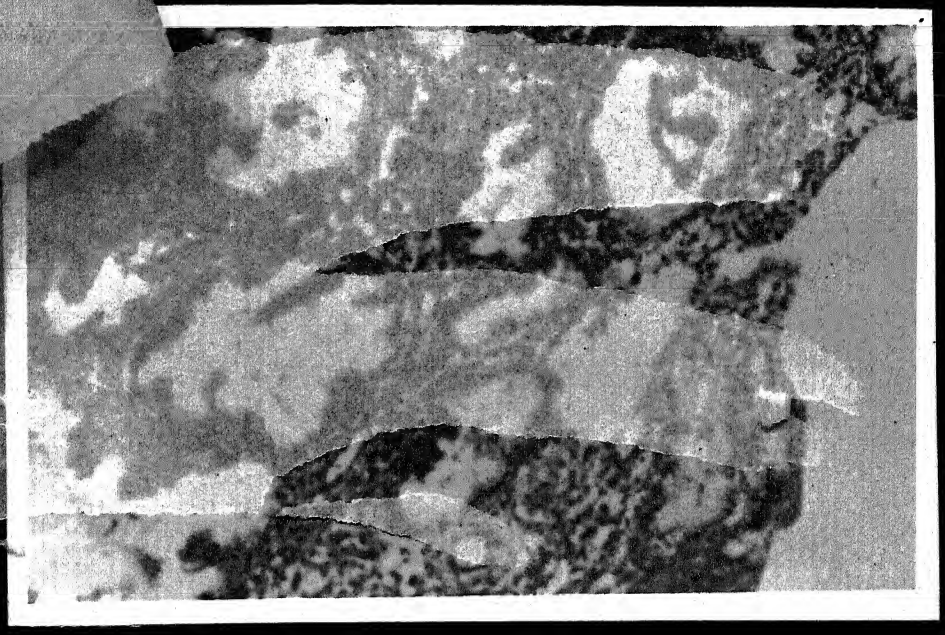
There was also a patients with hypothyroidism. They were given treatment for it and both conceived during treatment.



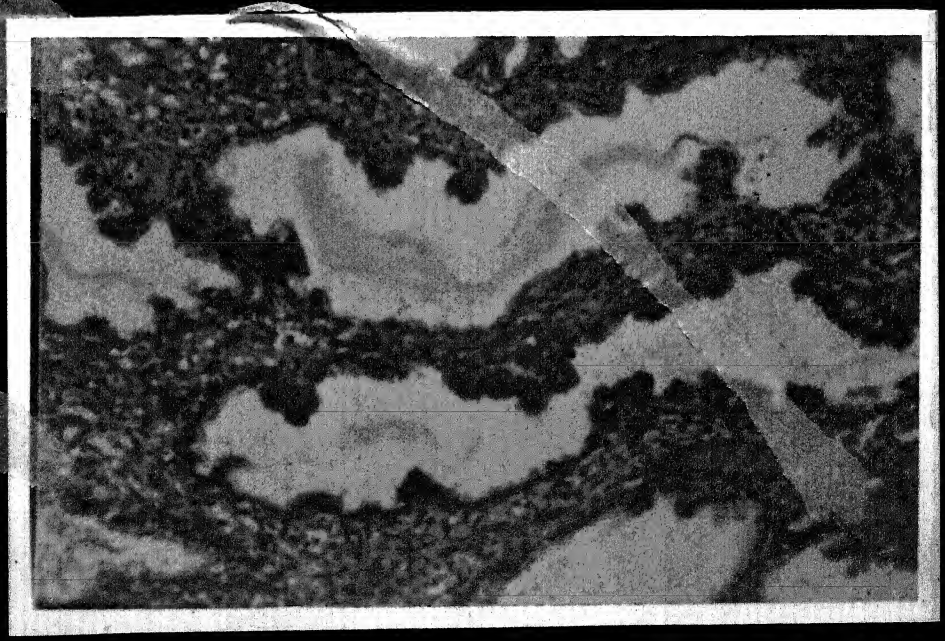
ENDOMETRIAL BIOPSY SHOWING
EARLY SECRETARY PHASE (1 x 10)



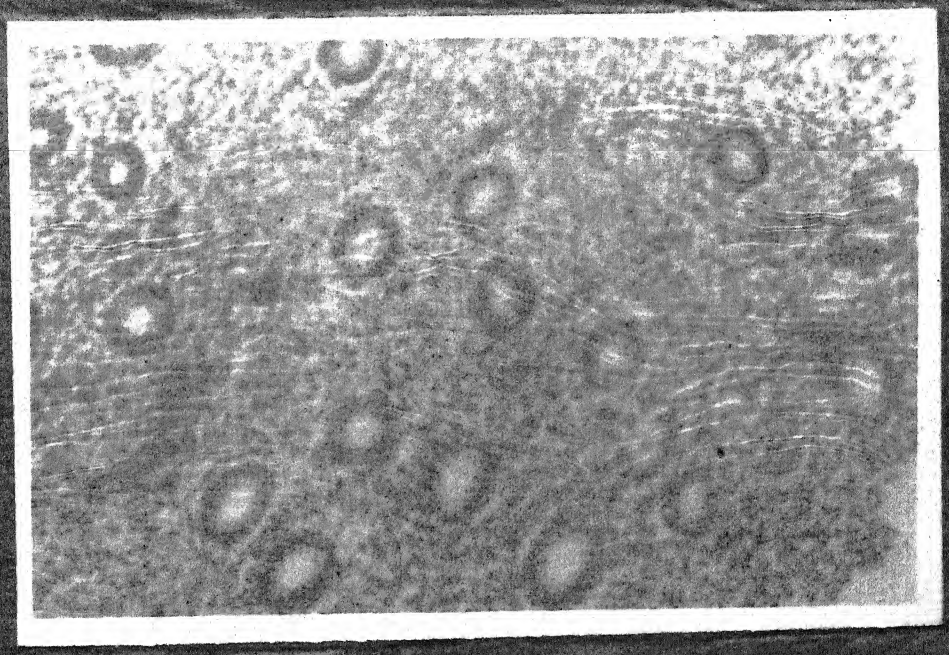
ENDOMETRIAL BIOPSY SHOWING
EARLY SECRETARY PHASE (1 x 50)



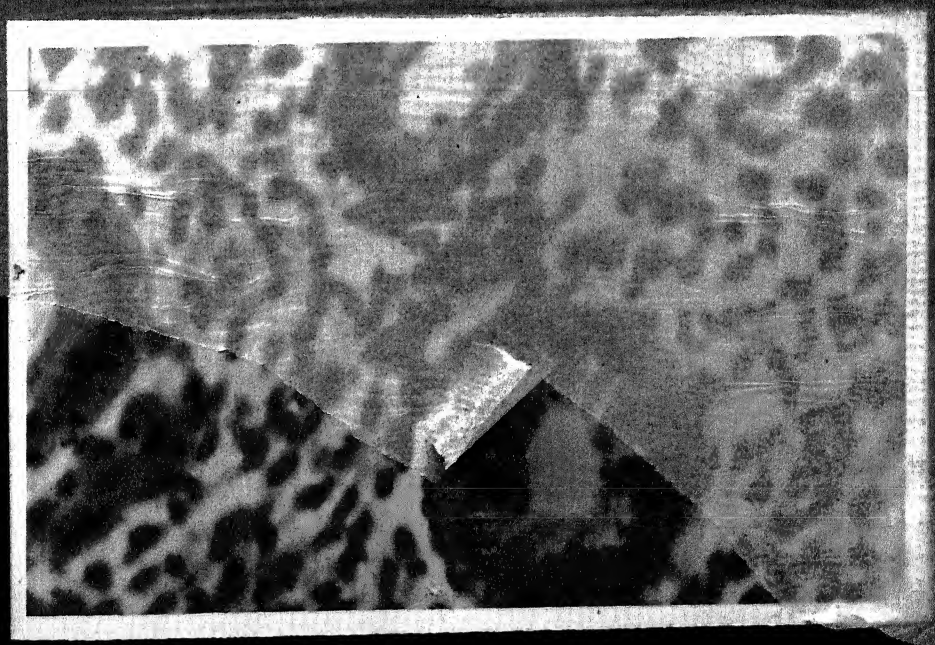
ENDOMETRIAL BIOPSY SHOWING
LATE SECRETARY PHASE (1 x 10)



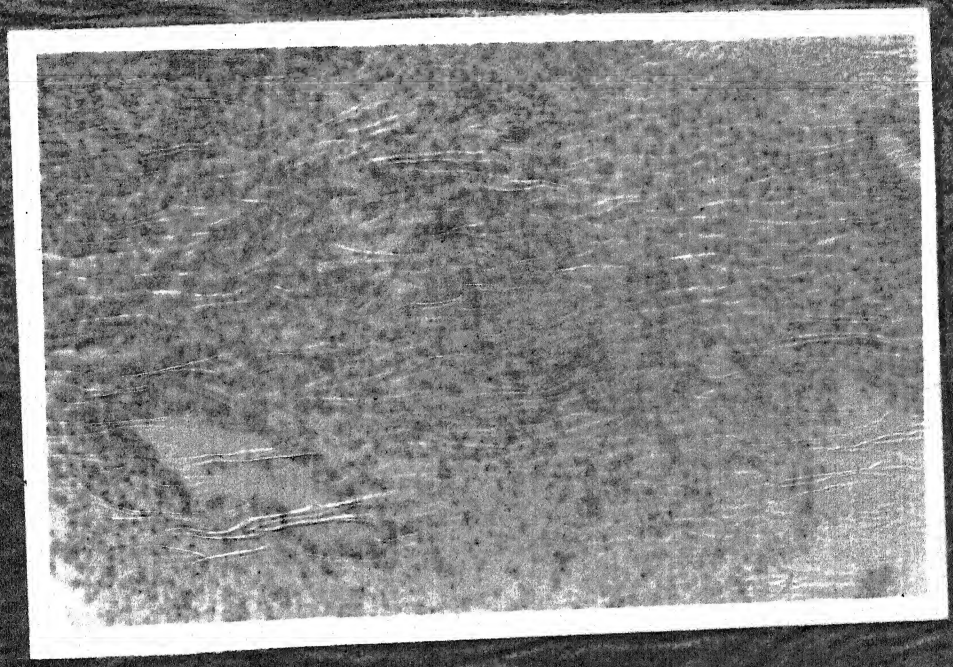
ENDOMETRIAL BIOPSY SHOWING
LATE SECRETARY PHASE (1 x 50)



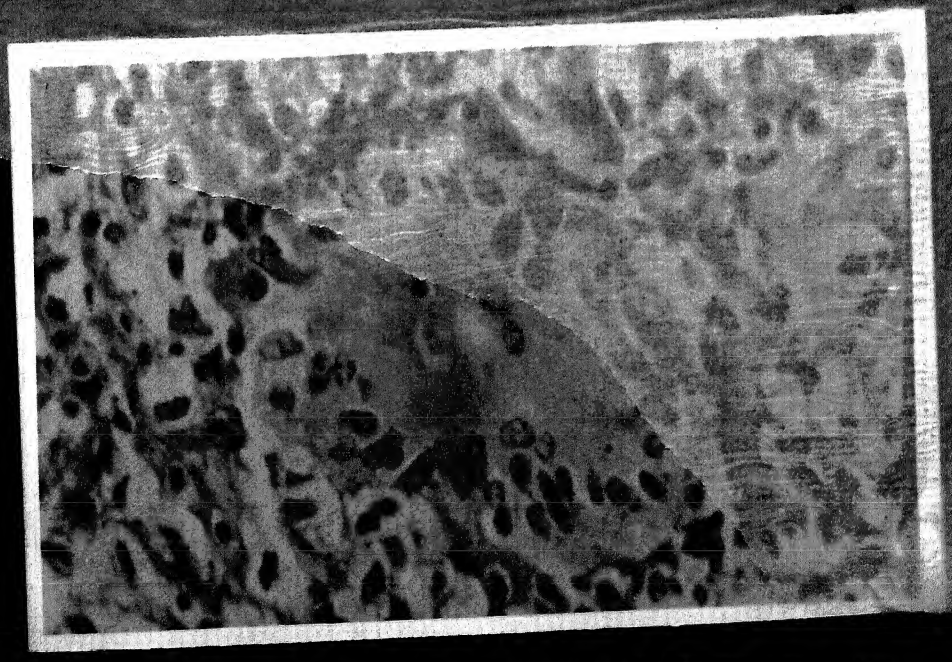
ENDOMETRIAL BIOPSY SHOWING
PROLIFERATIVE PHASE (1 x 10)



ENDOMETRIAL BIOPSY SHOWING
PROLIFERATIVE PHASE (1 x 50).



ENDOMETRIAL BIOPSY SHOWING
TUBERCULAR ENDOMETRITIS(1 x 10)



ENDOMETRIAL BIOPSY SHOWING
TUBERCULAR ENDOMETRITIS(1 x 50)

D I S C U S S I O N

D I S C U S S I O N

The present study was undertaken to determine ovulation by the easy, simple and cheaper procedures such as endometrial biopsy, cervical mucus examination and in some cases serial ultrasonography.

Detection of ovulation by these simple methods has also done by Birnberg (1958), Allende (1956), Ajjandi (1981) and Blackwell (1984).

In the present study 80% of the patients complained of primary intertility, 16% of secondary infertility and 4% of secondary amenorrhoea. The higher incidence of primary infertility in patients is probably due to the growing awareness among the general population for early conception and early treatment in the case of failure to conceive within one year of marital life.

The age group in which infertility was more common in the present study was 21-25 years (48%), 22% cases belonged to 16-20 years age group and 24% in the 26-30 years. This higher incidence of infertility in the 1st and 2nd decades of the reproductive life of a woman is probably due to early age marriage in our country. 54% of the cases in our study belonged to the lower middle socio-economic status. Though infertility is known to be more common in the higher socio-economic group. The higher incidence in the middle and lower group is because of the general

population around Jhansi belonged mostly to these groups. Only 5% of total patients attending the OPD are from higher strata of society.

Maximum number of cases (88%) belonged to the Hindu religion because is a basically Hindu community.

Though 52% cases belonged to urban areas it is not because of infertility is less common in rural areas. There is less awareness of the fact among the rural population that infertility can be treated and that it is not a curse of the God.

54% of the cases complained of infertility of 1-5 years duration. This was probably because the lesser duration of infertility the more people had hopes of conceiving very few cases belonged to the group with the duration of infertility of more than 10 years.

100% of the cases with polymenorrhoea and 75% with oligomenorrhoea had primary infertility. These cases with menstrual irregularities were found to have suffered from irregular periods over since menarche. 83% cases with normal menstrual cycles had primary infertility and cause infertility in these cases could either be failure to anovulate or due to other factors.

Hypoplastic uterus were found in 25% of polymenorrhoea and 25% cases of oligomenorrhoea and in 50% cases of secondary amenorrhoea. Patients with normal menstruation hypoplastic uterus was found in 8.33% cases.

Unilateral palpable ovary was found in 12.5% cases of oligomenorrhoea and 5.5% cases with normal cycles.

Bilateral palpable ovaries were found in 2.7% cases of normal cycles, 2.7% cases showed unilateral cystic ovary in patients with normal menstrual cycles. Vaidya et al (1978) reported 20% cases of hypoplastic uteri in oligomenorrhoea. They found one case of one ovary cystic and one case of both ovaries were cystic in hypomenorrhoea and none in oligomenorrhoea.

PREMENSTRUAL MOLIMINA

Molimina symptoms such as breast tenderness, headache, oedema and dysmenorrhoea are generally believed to occur in ovulatory cycles (Melody, 1961; Magyar et al, 1978). Our study dysmenorrhoea was present in 58.33% patients of ovulatory cycles. This is in accordance with the findings of Lamb et al (1953) who found it in upto 75% of cases. Pain was not a significant finding in anovulatory cycles, and it found in only 20% cases.

Breast tenderness was noticed in 22.22% of ovulatory cases and 10% in anovulatory cycles.

Abdominal fullness in the study cases was seen only in the ovulatory patients (27.77%) whereas 10% in anovulatory group.

Headache occurred exclusively in ovulating patients. It was found in 2.77% of ovulating patients. No patient complained of headache in anovulatory cases.

Mitteschmerz was found in only one(2.77%) case although the incidence as high as 35%. O' Herlihy et al (1980) has reported that this discrepancy can be explained on the ground that the majority of our patients belonged to rural background and poor literacy level and therefore the patients failed to report such symptoms as they did not attach enough significance to it.

CERVICAL MUCUS

Cervical mucus changes were found to be quite reliable in our study in detecting ovulation supported by Insler et al (1970). Similar experiences have been reported by Zondek Rozin (1954) and Malik et al (1979).

In our study, 14th day mucus samples in ovulatory group showed cervical mucus viscosity to be low in 30(83.33%) cases, moderate in 5(13.8%) and high in 1(2.7%) cases. These features of cervical mucus are obviously due to inhibitory action of progesterone on cervical glands after ovulation fully in accord with the observations of Zondek and Rozin (1954), Ronald and Mac Donald (1969).

In anovulatory cycles findings were reversed with viscosity at 14th day it was moderate in 25% and higher in 75% cases.

And ferning was also +2 to +4 in 10%, 30% and 60% cases respectively. This indicates the continuous unopposed action of oestrogen on cervical mucus due to persistence of graffian follicle and failure of ovulation to occur.

Malik et al (1979) in a similar study have reported premenstrual mucus minimum or negative ferning in 28.27% cases of ovulatory cycles. In anovulatory cycles they found complete or incomplete ferning in 53.10% and 27.22% cases respectively. These results though not similar, but are comparable to our own figures.

ENDOMETRIAL BIOPSY

Endometrial biopsy is the best single test for ovulation detection according to Moyees et al (1950).

It was performed in all cases in the present study. On the basis of histology, 72% showed secretary endometrium, 20% showed proliferative endometrium and 4% showed tuebercular endometritis.

Other workers have reported similar findings (Ajjandi et al, 1981 and Purandare et al, 1984).

On the basis of histology ovulation was diagnosed in 75% cases of polymenorrhoea and 62% cases of oligomenorrhoea. The groups of cases with normal menstrual cycle showed ovulation in 75.2% cases.

Anovulation was found in 25% cases of polymeno rrhoea, 37% cases of oligomenorrhoea and 50% of secondary amenorrhoea with lowest incidence in cases with normal menstrual cycle (22.22%).

Lower incidence of ovulation have been reported by Vaiday et al (1978). They found ovulation in 33% cases of oligomenorrhoea and anovulation in 12% cases.

Irrespective of the menstrual pattern anovulation was found in 20% cases in our study. Gupta et al (1980) and Saha (1961) have reported incidence of anovulation in 16.9% and 19.5% cases respectively. These findings are more or less similar to our findings.

Tubercular endometritis was seen in 4% cases in our study. Similar to that Saha et al (1961) reported it as 3% and Gupta et al (1980) reported a higher incidence of tuberculosis in 8.66% cases in his study.

ULTRASONOGRAPHY

On serial ultrasonography findings show that detection of ovulation by ultrasonography in comparison with endometrial biopsy is almost the same.

Our study showed that ovulation was detected in 97.22% cases with secretary endometrium and only 2.77% cases has no ovulation with secretary endometrium.

In proliferative endometrium 10% of cases had anovulation.

2 cases of anovulation conceived during the course of study who were taking the treatment for anovulation as ovulation induction (Clonifen citrate).

Hyperprolectinemia was found in 2 cases who were given treatment for it and out of 2, 1 conceived during treatment.

Hypothyroidism was found in 2 cases. They were given treatment and had conceived during treatment.

C O N C L U S I O N

CONCLUSION

Fifty patients of infertility either primary , secondary and secondary amenorrhoea were studied to determine ovulation by premenstrual molimina, cervical mucus, endometrial biopsy and ultrasonography.

The study consisted of 50 patients, 40 of primary infertility, 8 of secondary infertility and 2 of secondary amenorrhoea. All the patients were investigated with routine investigations and investigations to detect ovulation.

In brief it was concluded from this study .

1. Premenstrual molimina are associated with more commonly but not always with ovulatory cycles.
2. Cervical mucus is a good indicator of the cyclical changes in ovarian hormonal as no false positive results were found in the present study.
3. Endometrial biopsy is the mainstay in infertility studies as it provides information regarding the ovulating status. The degree of progestational effect and the possibility of other endometrial abnormalities like tubercular endometritis.
4. Serial ultrasonography for detection of ovulation is the confirmatory investigation, but it was very expensive for our poor population and result with

endometrial biopsy and ultrasonography were almost same.

5. The incidence of anovulation irrespective of menstrual irregularities was 20%.
6. Incidence of ovulation was found to be higher (75.2%) with normal menstruation than in those with menstrual disorder 62% to 75%.
7. The incidence of tubercular endometritis was found to be 4% in the present study.
8. Hyperprolectinemia was responsible about 20% cases of anovulation and effect of treatment was 50% (one patient conceived).
9. Hypothyroidism was responsible for about 20% cases of anovulation and effect of treatment was 100% (both patients had conceived).

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